U.PORTO
INSTITUTO DE CIÊNCIAS BIOMÉDICAS ABEL SALAZAR
UNIVERSIDADE DO PORTO

Small Animal Training Final Report

Integrated Masters Degree in Veterinary Medicine

SMALL ANIMAL MEDICINE AND SURGERY

Ana Maria Tomaz Coelho

Supervisor
Prof. Dr. Augusto José Ferreira de Matos

Co- Supervisor:
Dr. Alfred Legendre (University of Tennessee)
Dr. Jordi Manubens Grau (Hospital Veterinari Molins)

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Abstract

In order to complete my Integrated Masters Degree in Veterinary Medicine, I chose to participate in a three-week externship at the VeterinariMolins Veterinary Hospital in Barcelona. Following this training, I also took part in a thirteen-week externship in Tennessee, at the University of Tennessee College of Veterinary Medicine ("UTCVM"). These sixteen weeks of training were mainly focused on small animal medicine and surgery, and provided an opportunity to be closely guided and supervised by certified clinicians and specialists.

At the VeterinariMolins Veterinary Hospital I worked closely with certified veterinary physicians in performing consultations, identifying clinical signs, undertaking general and complementary examinations, as well as performing diagnostic exams in order to determine the patients' condition and illness, and propose a treatment plan. In cases where the surgical approach was warranted, I participated or observed in the procedure.

At the UTCVM, I participated in the Oncology, Ophthalmology, Community Practice, Nutrition, Anesthesiology, Dermatology and Neurology rotations. During this time, I acted as primary physician by taking full responsibility for my patients, performing patient rechecks, suggesting and completing chemotherapy protocols, participating in daily rounds, taking part in surgery and pre and post-surgical care, and suggesting and executing a anesthetic protocols. I also received training in spay and neuter procedures, where I was able to act as main surgeon, and also in discussions concerning scientific articles.

These experiences allowed me to put in practice the knowledge I acquired during my five-year studies, and I found myself to be fully fulfilled by the path I have chosen. Additionally, these externships allowed me to gain a better grasp of the Spanish and English languages, thus opening doors for my professional future.

Acknowledgments

I would like to express my gratitude to my family for providing me the opportunity to pursue my dream of becoming a Veterinary Medicine Doctor. I would like to specially thank my Parents, M. Angela Coelho and Francisco Coelho for being such an example of hard work and success. For having always believed in me giving me the strength and the advice I needed when I thought I was not able to accomplish my dream.

I am grateful to all my brothers and Sisters, Sofia, João, Nuno and Teresinha for all the complicity of being my big brothers and helping grow. The Coelho 5!

I am grateful to my dear niece Laura Tereno, for being “my person” supporting, earing and helping me no matter what or where.

I am grateful to my Dalila, for all this 14-years, for inspiring and showing me what was my path in this world. Because of you in at such young age I learned to love nature and respect all the beings equally. Looks like you want to live me now that your mission is done,, but I hope that you will stay with me longer because I still need you. There will never be another cat like you.

I am grateful to all my friends in all the cities in world where I have lived in, for enriching the experience of studding to be a veterinary doctor. Thank you Ana Maria Andrade, Mariana Machado, Sofia Norbrega, Joana Guimarães e Joana Bastos, Joana Cardoso, Ivone Silva, Marta Sousa and Cristinana justo.

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I would also like to acknowledge Dr. Legendre, Dr Smrkovsky, Dr Cain, Dr Narak and Dr Holford for teaching me and making me feel that I could go further in my future profession. I am grateful to all the members of the UTCVM for all their kindness, friendship and teachings.

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To ICBAS, for accepting me in and to all to all the teachers that helped me build the person and professional that I am today.

Abbreviation Index

½: Half
% : percent
<: less than
AR: aldose reductase
ARI: aldose reductase inhibitor
ASA: American Society of anesthesiologists
BID: twice a day
CNS: central nervous system
bpm: Beats per minute
DM: Diabetes Mellitus
DTM: Dermatophyte Test Medium
ECG: electrocardiogram
ERG: Electroretinography
ETCO2: End-tidal pressure of carbon dioxide
F: Fahrenheit
FeLV: feline leukemia virus infection
FIV: feline immunodeficiency virus infection

HD: hypersensitivity dermatitis
ICLE: intracapsular lens extraction
Kg: kilogram
Lbs: Pounds
IgE: Immunoglobulin E
LIU: *lens-induced uveitis*
min: Minute
mmHg: millimeter of mercury
mm: Millimeter
mg: milligrams
mL: milliliters

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AR: aldose reductase
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FIV: feline immunodeficiency virus infection
HD: hypersensitivity dermatitis
ICLE: intracapsular lens extraction
Kg: kilogram
Lbs: Pounds
IgE: Immunoglobulin E
LIU: *lens-induced uveitis*
min: Minute
mmHg: millimeter of mercury
mm: Millimeter
mg: milligrams
mL: milliliters

General Index

Signalment and motive for consultation: Spice is a 12-year-old female spayed canine Miniature Pinscher that was presented to the UTCVM Ophthalmology service for phacoemulsification surgery.

Anamnesis: Spice was diagnosed with diabetes mellitus (DM) by the referring veterinarian. Her DM is stable and currently well controlled. She receives 3 units of NHP Insulin SQ, bid, 30 min after every meal. The last fructosamine measurement made by the referring veterinarian (15 days before surgery) revealed a result of 324 umol/L (excellent range: 300-350 umol/L).

Spice´s first vision problems (bumping into objects and decreased level of activity) were noticed by the owners 2 month after with the diagnosis of DM. At the time she had mature cataract OD and immature cataract OS. She was seen with a mild lens-induced anterior uveitis that was managed with neomycin, polymyxin B and dexamethasone eye-drops, 1 drop OU, sid for 1 month. In order to evaluate if she was a good candidate for phacoemulsification, the referring veterinarian performed an ocular ultrasound (US) and electroretinography (ERG). (Appendix I) On US, bilateral primary intumescent cataracts were identified, anterior chambers were shallow and no retinal detachment was noticed. Spice´s ERG showed a normal retinal function OU. Spice was considered a good candidate for surgery and was referred to UTCVM. To date, she was being medicated with 0.03% flurbiprofen 1 drop OU sid. Her vaccines were up to date and she was dewormed. Spice lived in a house with a private garden, had no contact with other animals nor with toxic waste or garbage. Spice was fed with dry Hills W/D® prescription diet®. No other historic abnormalities were identified.

Physical Exam: Spice was alert with a normal behavior. She was overweight (4.8 Kg) and had a BCS of 8/9. She had a normal respiratory rate (44 rpm) and pattern and also normal heart and lung sounds. Her pulse was bilateral, symmetric, strong, and synchronous with a frequency of 108 p.p.m. Her mucous membranes were pink and moist with CRT<2 sec. Spice´s rectal temperature was 38ºC, and no parasites or blood were seen on the thermometer after retrieving it from the anus. Normal anal tonus was observed. A dehydration degree of <5% was noticed. All lymph nodes were within the normal limits. No abnormalities were found in her abdominal palpation. Ears showed no abnormalities. Lens opacification was noticed OU. Moderate dental tartar, mild stomatitis and several missing teeth were detected.

Ophthalmological exam: Spice had direct and consensual pupillary reflexes (PLR´s)**.** No orbital asymmetry was observed, the globes were normal in size and position with no strabismus. Lids and nictitating membrane were normally positioned and had a normal conformation. She presented normal palpebral reflexes and normal masticatory muscles. There was no ocular dischargeand bulbar conjunctiva was normal OU. To access Spice´s vision a menace reflex and cotton ball test were performed. She was blind OU, had absent menace reflexes and didn´t pay any attention to the cotton ball´s path. Slit-lamp biomicroscopy was used to exam the cornea, anterior chamber, pupil and iris. The corneas were clear, transparent,

convex and fluorescein negatives. The anterior chambers had no flair or other abnormalities, iris and pupil were also normal. Lenses had a normal position but were completely opaque. The Schirmer tear test was normal OU (22 mm/min OD and 20 mm/min OS; reference range <15mm/min). Intra-ocular pressures (IOP) were evaluated with applanation tonometry and the results were 4 mmHg OD and 6 mmHg OS, (reference range: 15-25 mmHg). These low values can be explained by the diagnosed lens induced uveitis. Indirect monocular ophthalmoscopy was used to attempt a fundic examination but, due to lens opacity, this was not possible.

Diagnostics: CBC: without abnormalities; Serum biochemical analysis: Hyperglycemia (Glucose: 124 mg/dL; Normal range: 84-120 mg/dL) hypercholesterolemia (Cholesterol: 504 mg/dL; normal range: 148-337 mg/dL). Urinalysis: without abnormalities

Problem List: Blindness, lens opacification OU, hyperglycemia, glycosuria, obesity and hypercholesterolemia.

Differential diagnosis: Lens opacity: Cataracts, nuclear sclerosis.

Blindness: Cataracts, retinal detachment, progressive retinal atrophy (PRA).

Diagnosis: Mature diabetic cataracts OU.

Treatment: 24h pre-operatory: 1%prednisone acetate, 0.03% flurbiprofen, 2.5% phenylephrine, 1% tropicamide and triple antibiotic solution (Neomicin, Polimixin, Gramicidin), 1 drop of each OU every 3 hours. Tepoxalin 50 mg, PO sid. Spice´s blood glucose was 75 mg/dL 30 min after feeding and no insulin was administered. 2h pre-operatory: The same topic drugs were administered: 1 drop of each OU every 30 min. Tepoxalin 50 mg PO Sid. Cefazolin 22 mg/kg IV was given 30 min before surgery and every 90 min until the end of it. Glycaemia of 354 mg/dL, 1unit of NPH was given. Phacoemulsification Surgery: In the left eye a foldable 13 mm 60-v prosthetic lens was injected into the empty lens capsule after the phacoemulsifier was used to ultrasonically liquefy and aspirate the lens using a “divide and conquer” technique. In the right eye the anterior chamber was shallow due to partial lens subluxation into the anterior chamber. Complete zonular disinsertion was noted from 3 to 9 o´clock. The capsulotomy was performed and hydrodissection was not done. Initially phacoemulsification was routine but after creating grooves and prior to nuclear removal, vitreous was noted within the lens capsule at 4-o´clock position. It was determined that intracapsular lens extraction (ICLE) would be necessary and the eye was left aphakic. Tissue plasminogen activator was injected intracamerally OU.

Post operatory: Spice spent the night in ICU. Triple antibiotic, 1% prednisolone acetate and a lubrication solution were administered every 4 hours. IOP´s were controlled 3 times, every 3 hours and were always normal (OD: 10 mmHg OS: 3 mmHg). First day post-operatory: 1 drop OU of: 1% prednisone acetate, 0.03% flurbiprofen, 1% tropicamide, triple antibiotic and dorzolamide hydrochloride and timolol maleate solution (cosopt®- Merck). Normal menace reflex was noticed OU. The PLR´s were not evaluated due to iatrogenic midriasis. In the anterior chamber +1 flare was present OU. Corneal edema was noticed in the right eye. IOP´s were 9

OS and 21 OD. No fundic abnormalities were noticed OU. Spice morning blood glucose was 504 mg/dL but because she did not eat her meal, only 2 units of NPH were given. Spice was discharged with prescription of: 1% prednisone acetate: 1 drop OU qid; 0.03% flurbiprofen: 1 drop OU qid; 1% tropicamide: 1 drop OU bid; triple antibiotic: 1 drop OU qid; lubricating gel: 1 strip OU qid and prednisone: 5mg PO sid for five days. After these five days, this dose should be decreased for ½ tablet sid for another 5 days. After this, ½ tablet should be given every other day for 5 days. Spice insulin administration routine (3 units 30 min after every meal) was restored.

1º week recheck: Normal menace reflex OU; Normal direct and consensual PLR OU. IOP´s: 13 mmHg OD and 15 mmHg OS. Schirmer test: 15 mm/min OD and 17 mm/min OS. Corneas: Clear and fluorescein negatives; Anterior Chamber: +1 flare OU; Iris and pupil**:** normal; fundic examination: no abnormalities OU. On Spice´s first week post-surgica recheck, she seemed to be enjoying good vision. The owner said that she was more active and was not bumping into objects anymore. A mild flare OU was noticed. Spice continued the same medication as previously described.

Assessment: The lens is an avascular, transparent and structured tissue with ectodermal origin that, in the normal eye, refracts incoming light rays on the retina. Lens disorders may be classified into abnormal embryologic development, abnormalities in transparency and lens position within the eye. The loss of transparency is a common denominator of all lens diseases. The transparency within the lens is maintained by complex factors: Low cytoplasm density, lack of intracellular organelles, absence of nuclei in the lens fibers, small spatial fluctuations of the refractive index of cytoplasm, and highly organized lattice arrangement of fiber cells. Those are influenced by cytoplasmic hydration, ionic strength and specialized metabolic functions in the lens (Gelatt 2007). The lens is rich in protein (35%) and water (65%) and poor in minerals. The proteins are divided into soluble proteins (crystallins) and insoluble (albuminoid) proteins (Ofri 2008). Cataracts formation is associated with pathologic alterations that increase albuminoids and decreases crystallins. As the cataract matures the hydrolytic and proteolytic enzyme activity increases (Gelatt 2007). The lens proteins break into polypeptides and amino acids that diffuse through the lens capsule into the anterior and posterior chambers. Also, the rapidly forming cataracts and the lens swelling (diabetes mellitus) cause small tears in the lens capsule. These molecules are not recognized by the eye's immune system because the embryology of the lens is such that the lens capsule isolates the lens from the immune system before birth. Therefore when the lens proteins enter in the aqueous, they elicit an inflammatory reaction known as *lens-induced uveitis* (LIU) that may be acute or chronic (Ofri 2008). This was described and treated by Spice´s referring veterinarian and explain the observed low IOP´s OU.

Throughout life, new lens cells are formed in the equator, forcing older cells toward the nucleus. The nucleus becomes denser and, when this becomes visible, it is called *nuclear sclerosis.* In

advanced cases nuclear sclerosis is similar to cataract and for this reason, it was our first differential diagnosis. The opacity found in Spice's lens did not allow the visualization of the fundus. This observation permits differentiating between the two entities. The retroillumination from the tapetum highlights the cataract opacities, distinguishing them from the transparent nuclear sclerosis. In most animals, nuclear sclerosis has a minimal effect in vision, the fundus can be visualized and menace is present (Ofri 2008).

Because the lens is avascular, its metabolic needs are met by the aqueous humor. Alterations in aqueous composition affect lens metabolism and transparency. Metabolism of glucose provides most of the energy requirements of the lens. Glucose enters from the aqueous by both diffusion and assisted transport. Most of the glucose is broken down anaerobically to lactic acid via the hexokinase (pentose phosphate) pathway, although some aerobic glycolysis occurs via the citric acid cycle. Elevation in glucose levels (in diabetic patients) inhibits the hexokinase enzyme. The glucose is diverted into the sorbitol shunt, where it is converted by aldose reductase (AR) into sorbitol (Gelatt 2007). The resulting hyperosmolality of the lens leads to fluid ingress. Initial changes include vacuole formation along the equatorial cortex that progresses to the anterior and posterior cortex. As more fluid enters the lens and the cataract matures, it may swell dramatically, this is a phenomenon known as an *intumescent cataract.* The swollen lens may push the iris forward, resulting in a shallow anterior chamber as seen in Spice´s eyes. This can also predispose to glaucoma because the iridocorneal angle is narrowed. The most prevalent ocular sign of diabetes mellitus in the dog is bilateral cataracts that may mature in a very short time course (days to weeks) (Ofri 2008). The diabetic cataract formation is dependent on the levels of AR. The use of aldose reductase inhibitors (ARI´s) showed to be effective in delaying the onset and/or progression of cataracts in dogs with DM (Kador *et al*. 2010). However this is not significant in lens with advanced changes like the ones noticed in Spice, and was not considered a viable treatment in her case. It may have a significant impact if used in dogs newly diagnosed with DM, if used continuously and indefinitely. For this to be successful good owner compliance is needed. (Kador *et al*. 2010)

The stage of development is the most used form of classification in canine cataract. It determines the extent of visual deficits, the onset of lens-induced uveitis, and the time of surgical intervention: *Incipient:* early, focal opacity with unaffected sight; *Immature:* more extensive opacity (most of the lens is involved). The transparency of the lens is reduced but not totally lost (tapetal reflection is still visible, but fundus may be partially obscured). Vision is affected but the animal is still visual; *Mature*: The lens is totally opaque and we have blindness. No tapetal reflection is noticed and the fundus cannot be examined; *Hypermature*: when mature cataracts progress into hypermaturity, they begin to liquefy (lens *resorption).* (Ofri, 2008) Based on this knowledge, on the fact that Spice had diabetes mellitus, and on her clinical signs (blindness, lenses generalized opacity), Spice was diagnosed with mature diabetic cataracts.

Surgical removal is the only method by which cataracts can be effectively treated, although surgical success is not guaranteed (success rates: 85% to 90%). Many dogs do not undergo surgery due to owner´s financial constraints, concurrent ophthalmic disease (e.g. retinal degeneration), or systemic disease that may preclude general anesthesia. Some owners prefer medical treatment or no treatment at all, when confronted with the potential complications of phacoemulsification (Lim *et al.,* 2011): Postoperative ocular hypertension (22.9%) corneal lipid opacity (19.0%), uveitis (16.2%) intraocular hemorrhage (12.3%), retinal detachment (8.4%) and glaucoma (6.7%) (Klein *et al.,* 2011). However, globe threatening complications are much higher in dogs receiving topical medical treatment or receiving no treatment at all when compared with dogs undergoing surgery (Lim *et al.,* 2011). Spice was diagnosed with cataracts before they had become mature. Failure rates for dogs receiving or not receiving treatment were higher in dogs with mature or hypermature cataracts when compared with immature cataracts. For this reason it would have been beneficial to have referred Spice sooner, before the cataracts became mature (Lim *et al.,* 2011).

The zonular instability observed during surgery may be present in hypermature cataracts, in older dogs, or be secondary to uveitis and intumescence of cataracts such as in diabetic cataracts (Ofri, 2007). No clinical signs of luxation were noticed before surgery. In the ocular US the anterior chamber was shallow bilaterally, but the lenses were still in their normal position. The treatment for dislocated lenses is the surgical removal through ICLE. The presence of lens in the anterior chamber can lead to complications such as pupillary block, glaucoma or corneal edema (Gelatt, 2007).

In order to maximize a successful surgical outcome, determining if the patient is a good candidate to phacoemulsification is essential. At first, the animal should be evaluated for systemic disease; secondly a good vision history and ophthalmic examination are required. Special attention should be paid to vision loss prior to the onset of cataract, or a history of nyctalopia (PRA suspicion). Patient temperament should be accessed because the exercise restriction after surgery and the administration of medications are essential for a successful outcome. Additional diagnostics include a B-scan US that is used to evaluate vitreal degeneration, retinal detachment, axial length of the lens and globe and the presence of spontaneous lens capsule rupture. An ERG is also indicated to determine retinal function and evaluate for the possibility of PRA. (Gelatt, 2007) The ERG in patients with Diabetes mellitus seems to have an amplitude reduction and timing delays of all components. Patients may have a reduced ERG preoperatively but a normal fundic examination and vision testing postoperatively. This suggests that ERG may be capable of detecting early diabetic retinopathy. (Safatle et al., 2010)

The goal of the preoperative therapy is to achieve mydriasis for surgical exposure, suppress ocular inflammation and minimize ocular microbial flora. The intraoperative complications of

ICLE and extracapsular lens extraction (ECLE) include fibrin accumulation, hemorrhage and vitreous expansion. In order to avoid fibrin, an intracameral injection of 25 mcg of tissue plasminogen activator (tPA) was used OU. Retinal detachment following ICLE is the second most common postoperative complication after secondary glaucoma. This is thought to be a result of preexisting retinal tears that enlarge following surgery, and disruption of the anterior hyaloid face may predispose eyes to this complication. The fact that the ICLE had been performed soon after the luxationmay decrease the chances for this complication (Gelatt, 2007). Spice is a successful case; she is able to see and did not develop any complication to date. The fact that she was aphakic OD means that she is severely hyperopic because of the loss of the refractive power of the lens. However the cornea is the major refractive organ of the eye so puzzlement vision is still possible even without an IOL.

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Signalment and motive for consultation: Quanto is a 6-year-old male castrated German Shepherd presented to the UTCVM's Neurology/Neurosurgery service due to a suspicion of lumbosacral stenosis.

Anamnesis: Quanto had a 9-month history of progressive hind limb lameness. At first, Quanto had occasional lameness that seemed to increase with exercise and resolve to some degree with rest. Three months before presentation the frequency of lameness increased until he was having problems daily. He was unable to jump, difficulting his job as a police dog. Quanto has had signs of fecal and urinary suspected incontinence for three weeks, the owner reported that Quanto urinated and defecated without posturing to do so. His left hind leg seemed weaker than the right, and he dragged his nails when walking. The owner has tried to treat Quanto with deracoxib (Deramaxx® Novartis) 1mg/kg sid but did not think it helped. Quanto was a police dog and lived with other animals. He was up to date on vaccines, dewormed and eating a high quality dry diet. He had always been healthy and no abnormalities were found when the owner was questioned about other systems.

Physical Examination: Quanto was alert and anxious. His body condition score (BCS) was 4/9, and weighed 36.4 kg. He had a normal respiratory rate (28 rpm) and effort and also normal lung and heart sounds. Quanto´s pulse was bilateral, symmetric, strong, and synchronous with a frequency of 68 ppm. His mucous membranes were pink and moist with a CRT of <2 sec. His rectal temperature was 39ºC, and no parasites or blood were seen on the thermometer after retrieving it from the anus; a normal anal tonus was also observed. A dehydration degree of <5% was observed in the patient. All lymph nodes were within the normal characteristics. No abnormalities were found in his abdominal palpation.

Neurological exam: Quanto had bilateral pelvic limb lameness and was knuckling his left hind foot when walking. He displayed a bunny-hopping gait when running up stairs. He had normal cranial nerves. He presented a delayed proprioceptive positioning response. The other postural reactions were accessed and no abnormalities were found. He had a decreased flexor withdrawal reflex in his left pelvic limb but all other reflexes were normal. He was painful in his lumbosacral area and had mildly decreased muscle tone in his left hind limb. Pain was accessed by direct pressure over his lumbosacral joint, rectal palpation and elevation of his tail. Quantos lesion was localized to the L4-S2 spinal segments or his cauda equina nerve roots.

Problem List: Bunny hopping up stairs, decreased left flexor withdrawal reflex, delayed proprioceptive positioning response, suspected incontinence, lameness, knuckling left foot while walking.

Differential Diagnosis: Degenerative lumbosacral stenosis (DLSS), diskospondylitis, neoplasia, and external injury, arthritis, hip dysplasia and cranial cruciate ruptures.

Diagnostics: Radiographs: normal hip joints; normal L7-S1 intervertebral space and possible osteochondrosis of the cranial endplate of S1. MRI: severe dorsal and ventral stenosis of the

lumbosacral junction; stenosis of the intervertebral foramen at the level of the left L7 nerve root. CBC: within the normal limits Chemistry panel: No abnormalities were noticed.

Diagnosis: Degenerative lumbosacral stenosis and left foraminal stenosis.

Treatment: Surgery: Dorsal laminectomy with removal of mineralized disc material and foraminal decompression. The IVD was swabbed for bacterial culture due to the presence of fibrillated cartilage in the L7 and S1 endplates that suggested the possibility of diskospondylitis. Swabs were submitted for aerobic and anaerobic culture, and no growth was seen in 4 days. The bony protuberance reported on MRI was seen on the craniodorsal aspect of S1 but it was not possible to remove it due to its localization beneath the spinal nerves. After surgery, Quanto was able to walk without knuckling. He was urinating and defecating normally and appeared to be comfortable. Quanto was prescribed six weeks of crate rest, gabapentin 10mg/kg PO tid, tramadol 3mg/Kg PO bid and carprofen 2mg/kg PO bid for pain management.

Assessment: The spinal cord and the vertebral column grow at different rates during embryonic development. The spinal cord is derived from ectoderm and is shorter than the vertebral column, derived from mesoderm. In the majority of dogs, the *conus medullaris* is located in the caudal half of L6 or cranially in L7. At this point, it originates the cauda equina, composed by the L6, L7, S1-S3 and Cd1-Cd5 nerve roots, and located between L6 and Cd5 (Meij & Bergknut 2010). Ventrally, the cauda equina is protected by the dorsal longitudinal ligament, the L7-S1 intervertebral disk (IVD) and vertebral bodies. Laterally it is bound by the L7 and S1 pedicles and intervertebral foramina. Dorsally it is covered by the interarcuate ligament and the laminas of L7 and S1. The articulation between L7 and S1 is made by the IVD and the synovial facets. It is stabilized by the ventral and dorsal longitudinal ligaments, the interarcuate ligament, the interspinous ligament and finally by the sacral fascia and epaxial muscles (Meij & Bergknut 2010).

DLSS is the most common disorder of the lumbosacral junction seen in middle-aged large-breed dogs, especially in male working German shepherd dogs (GSD). DLSS is caused by a combination of anatomic factors that result in the compression of the cauda equina and its blood supply. Abnormal motion of the lumbosacral junction due to repetitive stress, genetic and/or congenital abnormalities (symmetric or asymmetric transitional or extra vertebrae) seem to predispose to L7-S1 disk degeneration (Meij & Bergknut 2010). Dogs with transitional vertebrae segments (TVS) have a higher risk of developing this disease due to malarticulation that can cause a dysplastic disk, prone to premature degeneration (Worth *el al*. 2009). Altered joint facet orientation was also proposed to cause an abnormal degree of motion of the intervertebral articulations, producing mechanical stress in the IVD. German shepherds have distinct geometries of the articular facets and a variable asymmetry between the left and right articular facets. This may change the weight distribution and explain the predisposition of GSD to DLSS (Worth *et al.* 2009). Sunwankong *et al.* (2008) concluded that the angles of the L7-S1 joint were

more sagittally oriented in GSD than in other breeds and that this could affect the lumbosacral motion. However, they were not able to find a relationship between this abnormality and the incidence of disk degeneration.

The IVD degeneration begins with the degradation of proteoglycans. Subsequently, the water and nutritional supplies diminish and the disk loses its width. The unstable spinal segment changes the weight bearing from the central axis of the IVD to the peripheral parts of the spine, the joints facets and ventral aspect of the vertebral bodies. A ventral subluxation of S1 can occur and contributes to more compression (Meij & Bergknut 2010). Although this was considered a signal of lumbosacral instability seen in the majority of dogs in one study, the size of the step did not correlate to clinical signs (Sunwankong *et al*. 2008). In order to compensate for the increasing instability, a proliferation of the soft tissues occurs (hypertrophy of the interarcuate ligament and joint capsules and epidural fibrosis). The cartilaginous end plates thicken and osteophytes and ventral spondylosis can form. All of this contributes to the abnormal disk nutritional supply. The narrowing of the IVD and the loss of *annulus fibrosus* (AF) tensile strength causes bulging of the AF and Hansen II herniation (Meij & Bergknut 2010).

The most common clinical signs of DLSS are lumbar pain, difficulty rising (that can be confused with hip dysplasia and orthopedic disorders) and recurring lameness of one or both pelvic limbs. The inability to jump and difficulty in climbing stairs are also described. Exercise usually exacerbates the signs secondary to intermittent claudication and may resolve to some degree with rest. The fact that lameness worsens with exercise and resolves to some degree with rest can be indicative of neurogenic lameness. This is due to failure of arterial vasodilatation in the affected nerve roots during exercise because of compression. Pelvic limp paresis only occurs in advanced cases. Because there may be pain with no neurological deficist and it may be difficult to distinguish pain associated with spinal disease from the one caused by orthopedic problems. Eliciting pain with over the lumbosacral joint supporting the animal´s pelvis, lifting its feet or by rectal palpation can help to differentiate lumbosacral pain from orthopedic disease. Pain can also be elicited by the elevation of the tail and than rotating the lumbosacral joint by swinging the hind limbs. (Sharp & Wheeler 2005)

Only in later stages the disease progress to paraparesis. The weakness involves the muscles innervated by the sciatic nerve, so a decreased extension of the hock and a plantigrade stance are noticed. Fecal and urinary incontinence are related to compression of the sacral nerves (pelvic and pudendal nerve dysfunction) the urinary incontinence is of the lower motor neuron (LMN) type, characterized by dribbling of urine and a bladder that is easily express by manual pressure. Fecal incontinence seems to be related with poor anal tone, which can be present even with an intact anal reflex. (Sharp & Wheeler 2005)

Key to clinical diagnosis is the localization of pain in the lumbosacral region without painful hip joints although diseases like neoplasia, diskospondylitis and synovial cyst(s) compressing the

lumbosacral area present similar clinical signs. Orthopedic diseases such as arthritis, hip dysplasia and cranial cruciate ruptures are also differential diagnoses (Lorenz *et al*. 2011).

Clinical signs and anamnesis were important to define Quanto´s hind limb lesion as chronic progressive and bilateral. With the neurological examination we were able to localize it.. Because Quanto had normal bilateral patellar reflexes, we were able to localize the lesion caudally to L6. However the patellar reflex can be exaggerated when the sciatic nerve is depressed. This phenomenon is called pseudo-hyperreflexia and is due to decreased tone in the muscles innervated by the sciatic nerve wich are responsible for counteract the extension of the stifle that is induced by the patellar reflex. This pseudo-hyperreflexia must be differentiated from the increased patellar reflex that happends with upper motor neuron deficits, in lesions cranial to L4 segment (Sharp & Wheeler 2005). The withdrawal reflex of the pelvic limb evaluates primarily the sciatic nerve and its spinal cord segments (L6, L7 and S1). The motor response of this reflex is the flexion of all joints, except the hip, controlled by the femoral nerve (Lorenz *et al*. 2011). Quanto had a normal right flexor reflex but decreased flexion on the left side. This is a LMN sign that made us suspicious of a possible sciatic lesion. The gastrocnemius reflex and cranial tibial reflexes were normal bilaterally so we concluded that it was not a complete sciatic nerve lesion. The perineal reflex was normal. It tests the branches of the sacral plexus that are located in the pelvic canal. It is the best indication of the functional integrity of the sacral spinal cord segments and nerve roots. Testing this reflex is especially important in animals with urinary bladder dysfuncion. Quanto was suspected of having LMN incontinence because he did not posturate for urination and defecation but this could also be lumbosacral pain related. The fact that he was defecating and urinating normally after surgery and the normal perineal reflex made us conclude that quanto has not incontinent. Quanto also had a bunny-hopping gait when running up the stairs. No specific location explains this clinical sign, but it may be related to lumbosacral pain.

At this time, our major suspicion was a lesion at L7-S1. Imaging was the first approach to rule out bone-associated neoplasia, diskospondylitis, trauma and vertebral abnormalities (Worth *et al.* 2009). Plain radiographs showed no hip joint abnormalities (Appendix II-1). Also, fractures, TVS, spondylosis, subluxation of S1, and signs of infectious or neoplastic disease were not identified lombo-sacral vertebral column. The L7-S1 intervertebral space did not look narrowed on radiographs but osteochondrosis of the cranial endplate of S1 seemed to be present. The superimposition of the iliac wings and iliosacral joints made it difficult to detect a small lesion such as this on survey radiographs (Appendix II-2).

In studies, a correlation between neurologic and radiologic findings was not found. Neither the width nor the lumbosacral joint angle, nor its malalignment were significantly different between dogs with normal and abnormal neurological signs. Also, the step lesion between L7 and the sacral canal (S1) has been reported to be present in 69% of dogs with DLSS, but it was also

seen in healthy dogs. (Worth *et al* 2009).

Myelography is considered by many to be useless in DLSS diagnosis because the dural sac terminates cranially to L7 in many dogs. However, the contrast column may cross the lumbosacral space in normal and affected dogs. In these dogs, it could be a useful diagnostic when CT or MRI are not available. The major limitation of this is the inability to see the compression of nerve roots in L7 (Worth *et al* 2009).

A CT study is a good diagnostic tool, its advantage being the ability of reformatting dorsal and sagital images from transverse planes. However, MRI is the most sensitive for detecting disk degeneration, attenuation of normal epidural fat and the compression of nerve roots. Despite the advances in imaging diagnostics, CT and MRI results are not as important as clinical signs and surgical factors determining prognosis. No correlation was noticed between the severity of compression and the severity of clinical signs (Worth *et al.* 2009).

A MRI study was considered diagnostic in Quanto´s case. A severe extradural compressive lesion caused by T1 and T2 hypointense tissues was noticed in the L7-S1 intervertebral disc space. Severe compression of the spinal nerve roots was also identified. Except for the L7-S1, all lumbar intervertebral disks were well hydrated (high signal on T2 sequences). This lesion was a dehydrated disk protrusion. The cranial endplate of S1 was flattened and irregular at its dorsal aspect. There was sclerosis of the cranial endplate of S1, characterized by T1 and T2 hypointensity. On the proton weight density transverse sequence, there was a separate ovoid fragment at the craniodorsal aspect of S1, lying in the left ventral aspect of the vertebral canal (Appendix II-3).

Surgical and conservative treatments are described for the treatment of DLSS. The management this disease is based on the evaluation of the severity and duration of the clinical signs. Conservative management is indicated only for the first episode of pain or in cases of intermittent pain. Confined cage rest for 4 to 8 weeks and pain management with non-steroidal anti-inflammatory drugs leads to a recovery rate of 24% to 50%. Signs often recur when exercise is resumed (Lorenz *et al*. 2011). Injections of methylprednisolone sodium acetate into the lumbosacral epidural space were described as having shown improvements in 79% of the patients (Meij & Bergknut 2010). For this to be successful the dogs cannot have proprioceptive deficits or urinary nor fecal incontinence. This is a controversial treatment due to corticosteroid side effects like lowering the immune response predisposing to the flare up of unrecognized diskospondylitis (Meij & Bergknut 2010). The conservative approach is not curative for the underlying cause, but may yield good pain management. This was not an option in Quanto´s case because he already had neurologic signs.

Surgical treatment is indicated when the conservative management fails or when neurologic deficits are present. Dorsal laminectomy is the most commonly reported surgical technique. This procedure allows for decompression and visualization of the cauda equina. The nerve

roots can be retracted laterally for visualization of the disk for diskectomy and relief of compression. Dorsal laminectomy has a short-term successful outcome of 41% to 78% (Lorenz *et al*. 2011). Laminectomy alone does not cause instability of the lumbosacral articulation but the sum of diskectomy reduces stability (Lorenz *et al*. 2011). When laminectomy alone may not provide enough decompression, techniques like partial discectomy, foraminotomy and facetectomy are required for the enlargement of the foramen. The removal of the articular processes should be avoided because this is likely to increase limbosacral instability. Foraminotomy alone can be performed in cases were the core problem is nerve root compression without spinal canal stenosis (Meij & Bergknut 2010). Endoscopic assistance has been described to improve intra-operative visualization and avoid the risk of incomplete decompression (Worth *et al.* 2009). Stabilization by fixation and fusion is indicated in dogs with S1 subluxation or to prevent further development of lumbosacral instability (Meij & Bergknut 2010).

Good postoperative management is essential for a successful outcome. It consists in restricted exercise for at least six weeks. Nonsteroidal analgesics may be given to reduce pain during the postoperative period (Lorenz 2011). Physiotherapy during rehabilitation can improve long-term functional outcome (Meij & Bergknut 2010).

Prognosis is fair to good when clinical signs improve with surgery and if surgical intervention is performed early. Recurrence rates are between 3% and 18% in the working dogs. Severe neurological deficits, urinary and fecal incontinence for more than a few weeks before surgery are negative prognostic factors. Those animals and have a guarded to poor prognosis. (Lorenz *et al*. 2011). Quanto was considered to have a excellent prognosis for return to normal ambulation and comfort and good prognosis for return to normal working level due to his fast recovery after surgery. However being a working dog the possibility of recurrence should be considered

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Signalment and motive for consultation: Pat T Cat is a 13-year-old male castrated American domestic shorthair cat, presented to UTCVM's Dermatology Service for evaluation of a history of intensive pruritus. This was his second recheck; furthermore he was presented for allergy testing.

Anamnesis: Pat was described as to being seasonally affected (spring and fall). The patient also had a history of responding well to corticosteroid injections (Methylprednisolone). He lives with 5 other cats, strictly indoors, with no recent additions of new cats. Pat was vaccinated but not treated for internal or external parasites. He supposedly doesn't have access to toxic waste or garbage. No abnormalities were identified concerning other systems. His referring veterinarian started Pat and the other household cats on a food trial with Royal Canin hypoallergenic® diet and administered Methylprednisolone 5mg/kg SQ on the same date. The owners described an initial response to the treatment and food trial, but after approximately 1 month Pat began showing signs of intense pruritus again. Pat's physical exam showed him as alert and with all vital parameters within normal limits. He weighed 4.9 Kg. His dermatologic exam revealed extensive excoriated, crusted and erythematous areas of alopecia over the neck, dorsum, abdomen, and periocular, periauricular and axillar areas. He also had miliary dermatitis on his dorsum and an indolent ulcer on his upper lip. In addition, his ears were erythematous and excoriated, and moderate brown ceruminous debris was observed in the external ear canal. A Wood lamp was initially used to attempt to visualize fluorescence of dermatophytosis; results were negative. A fungal culture (DTM) was submitted along with full blood work (CBC and Chemistry) including a FeLV/FIV test. Superficial and deep skin scrapings, along with tape cytologies and impression smears, were also performed in the hope of identifying *Demodex gatoi* or *cati*, *Notoedres cati*, *Cheyletiella*, or bacterial and yeast organisms. All the tests were negative. In the skin impression tests, cocci, *Malassezia*, neutrophils and occasional eosinophils were observed. The blood work showed leukocytosis (left shift neutrophilia) and eosinophilia. Eosinophilia could be secondary to Pat's allergic disease and possible parasitosis. Left shift neutrophilia could be due to the inflamed excoriated skin lesions, considering he was not showing evidence of systemic disease. Based mainly on the skin cytology evaluation Pat was diagnosed with superficial pyoderma, *Malassezia* dermatitis and bilateral otitis externa (bacterial and yeast). Since all the other pruritic causes were excluded, Pat´s superficial pyoderma and yeast ear infection were thought to be secondary to allergy. Because Pat's owners had difficulty administering oral medications, he was given cefovecin sodium (Convenia®- Pfizer) 7mg/kg SQ. Convenia injections were prescribed to be administered by the referring veterinarian every two weeks until 2 weeks after the pyoderma was cured. This particular antibiotic was selected mainly for the owner's convenience (relatively long lasting effect of this drug allows for dosing every two weeks) and its broad spectrum. In order to address his current pruritus, Dexamethasone Sodium Phosphate at

2mg/kg SQ was administered once at presentation. This corticosteroid was specifically selected for its shorter action span (up to 7-10 days), in order to make intradermal and/or serum testing possible in the future. Pat was discharged with instructions to begin a flea and otodectic, notoedric, and cheyletiella mites trial, using topic selamectin every 2 weeks for a total of 3 consecutive treatments. He was also prescribed Cyclosporine A (or CsA) at 7 mg/kg PO, SID as an immunomodifying agent. To assess the ear problem Otomax®-merck (gentamicin, betamethasone and clotrimazole) at 0.5 mL AU BID was prescribed for 10 days. Furthermore, in order to treat Malassezia a shampoo with chlorhexidine, acetic acid and ketoconazole was prescribed to be used twice a week. The food trial, at this point, was stopped, both to avoid interference with diagnostic tests previously described and because the immunosuppressive therapy would render the results from a food trial interpretable

Four weeks after the first visit, Pat had his first recheck. Less intensity of pruritus (6-7/10) and some hair regrowth in the lesions were noticed. A new ear cytology also showed improvement. No bacteria were found, and *Malassezia* were now only identified in his left ear. The skin surface cytology still revealed a heavy burden of neutrophils and bacteria (intra/extracellular cocci). The blood work revealed left shift neutrophilia, eosinophilia and monocytosis. Chemistry panel remained normal. A skin culture was performed and the results of this test showed that the organisms (*Staphylococcus aureus*) were sensible to cefovecin. Under this notion the patient was continued on Convenia. Skin and serum allergy testing were considered and corticoid medication was not repeated. Ciclosporin and selamectin treatments were continued with the same frequency. A 1.5% lidocaine spray and a pramoxine and calamine lotion was prescribed for the relief of pruritus. Ten days later Pat had his second recheck exam for allergy testing.

Physical Examination: Pat was alert and showing a normal behavior. His body condition Score (BCS) was 5/9, and weighted relatively the same (4,6 Kg). Normal respiratory rate (28 rpm) and effort (his respiratory movements were costo-abdominal, regular and the relation between inspiration and expiration was 1:1.3, with no use of the accessory muscles of respiration), and also normal lung and heart sounds. Bilateral, symmetric, strong and synchronic pulses with a a frequency of 168 p.p.m were also observed. Pink and moist mucous membranes with a CRT <2 sec. His rectal temperature was 38ºC, and no parasites or blood were seen on the thermometer, a normal anal tonus was also observed. A dehydration degree of <5% was observed in the patient. All lymph nodes were within the normal limits. No abnormalities were found in the abdominal palpation. Multiple skin lesions were found (described in dermatological examination).

Dermatological Examination: His dermatologic exam revealed improvement since the last visit, but Pat still had extensive excoriated, desquamate, erythematous areas of alopecia over his temporal, abdominal, axillar and inter-digital areas although some hair regrowth over these

lesions was noticed. Lichenification was seen on the neck, miliary dermatitis was identified on his dorsum and an indolent ulcer was present on his upper lip. No parasites were seen and normal epilation and normal to dry skin. A decreased in the intensity of the patient's pruritus was evident (now 5/10).

Problem List: Pruritus 5/10, alopecia, erythema, excoriation, desquamation, indolent ulcers and miliary dermatitis.

Differential Diagnosis: Food allergy; Flea and/or Mosquito bite hypersensitivity; Dermatophysosis; Ectoparasites (Cheyletiellosis, *Otodectes cynotis*, demodecosis or feline scabies); Cutaneous lymphoma; Psychogenic alopecia; Pemphigus.

Diagnostics: Allergy skin test: Negative; Serum allergy test: oak mix +++, quack +, perennial rye +, Timothy +, red top +, the rest of tested allergens were negative.

Diagnosis: Atopy and secondary superficial pyoderma.

Treatment: Chlorpheniramine 2-4mg sid or bid as needed, Selamectin topically every 3 weeks, 1.5% lidocaine spray topically in the itchy areas tid, cyclosporine 100mg/mL 25 mg SID, pramoxine and calamine lotion in the lesions as needed.

Assessment: Based on Pat´s history of seasonal and steroid responsive pruritus, either a flea and/or environmental allergy were suspected. Although other pruritic causes such as flea and mite infestations (*Demodex gatoi* or *cati*, *Notoedres cati*, *Cheyletiella*) or dermatophytosis (*M. canis, M. gypseum,* and *T. mentagrophytes*) were considered. Dermatophyte infections are often self-limiting and cats usually have a poor inflammatory response. This explains the relative tolerance for *M. canis*, and the high rate of asymptomatic or subclinical carriage of this species among cats. Pruritus is usually minimal or absent in fungal infections however, it could occasionally be marked suggesting ectoparasitism, allergy or secondary bacterial (usually staphylococcal) infection (Muller *et al*. 2001). This was excluded by Pat´s DTM and woods lamp negative results.

To diagnose the presence of feline mites (*Demodex cati*, *D. gatoi, Notoedres cati and Cheyletiella)* superficial and deep skin scrapings were made, but were negative. Ear cytology was performed and no ear mites were identified. Skin scrapings are diagnostic for these conditions but mites can be difficult to find in cats that groom excessively, therefore a short therapeutic trial is indicated before more complicated testing are undertaken (Muller *et al*. 2001). Based on this, selamectin pipettes were used (3 with 2 week interval) with no significant improvement. *D. gatoi* could still be a possibility as selamectin is not an effective treatment. A lime sulfur dip trial weekly for 6 weeks would be needed to be ruled out. Since none of the other cats were affected and the pruritus was long-standing with seasonal exacerbation and glucocorticoid-responsive. A mite infestation was ruled out but the possibility of having a *D. Gatoi* infestation could be considered in the future depending on the patient´s response (Muller *et al*. 2001).

Feline atopy is a type I hypersensitivity reaction to environmental antigens (allergens) manifested mainly as a pruritic skin and/or respiratory disease in cats. It is caused by an exaggerated or inappropriate response of the affected cat to these environmental allergens (Muller *et al*. 2001). IgE is supposed to have a pivotal role in these conditions but this has not been sufficiently studied in cats. Allergen-specific IgE has been detected in the serum of allergic cats, but also in healthy cats. Non-IgE mediated reactions may also play a role in the development of hypersensitivities in cats. Feline atopy can be seasonal or non-seasonal, depending on the offending allergens. The most common environmental allergens are non-seasonal. House dust mite reaction (predominantly *Dermatophagoides farinae*) is the most prevalent. A genetic or heritable predisposition is suspected. The incidence of the disease is controversial; some say it is the most common cause of allergy in cats (73% of all allergic cats) or that it is second in incidence to fleabite hypersensitivity (Muller *et al*. 2001). Clinical signs develop at 6 months to 3 years old, and no breed or sex predilections were demonstrated. The clinical hallmark of atopic dermatitis in cats is glucocorticoid responsive pruritus. The type of skin lesions can vary and clinical manifestation is influenced by the duration of disease, intensity of pruritus, and the cat´s behavior. Skin lesions often described include erythema, papules and crusted papules (miliary dermatitis), excoriations and linear crusts, exudative lesions, and eosinophilic plaques and self induced alopecia or hypotrichia. Eosinophilic plaques may occur as single lesions (abdominal area and in the medial thighs) but are often found together with other lesions. Eosinophilic ulcers (upper lips) and eosinophilic granulomas (face, head and chin) are less common signs of atopy. Lesions are usually found in a symmetrical pattern that often includes head, pinnae, neck, abdomen, flanks and limbs. The head lesions occur at the preauricular or periocular areas. Erythema and hypotrichia around the lower lips and chin can be confused with signs of acne. The incidence of concurrent allergy is unclear but the presence of fleabite hypersensitivity and/or food hypersensitivity can greatly complicate the diagnostic work-up as well as the therapeutic regimen. Lymphadenomegaly may be found as a sign of chronic skin inflammation. Sneezing is reported to be present in 50% of the cases. Chronic coughing and asthma may occur, although bronchial hyperreactivity has not been proven to be higher in cats with atopy when compared to other allergic diseases (August 2006). These clinical presentations are not considered pathognomonic for hypersensitivity dermatitis (HD), and the diagnosis of those diseases is usually based on the exclusion of other pruritic pathologies. Additionally, responses to dietary restriction, flea control or immune-modulating therapy (allergen-specific immunotherapy, glucocorticoids or CsA) are necessary to establish the etiological diagnosis of food-associated HD, fleabite HD or atopy. The large phenotypic variability of feline non-flea HD has complicated the establishment of definitive diagnostic criteria for this disease (Favrot *et al*.2011). Cats with non-seasonal HD should undergo a 6-8 week restriction diet to determine the importance of food allergens in the development of the

condition and to identify which are the ingredients responsible for the allergic reaction. Allergen-specific intradermal and/ or IgE serological testing can be used to recognize environmental allergens (Hobi *et al. 2011*). The IgE serum test is considered an unreliable test for atopy in cats, as it was proven to be influenced by age, flea control, and deworming status. However it is beneficial for the selection of allergens for allergen-specific immunotherapy (Belova *et al.*2012). A definitive diagnosis for feline atopy requires a positive intradermal allergy testing (IDST), but this requirement is not met in some atopic cats, like Pat, because reactions, including those to histamine, are subtler than in dogs. This may be because IDST in cats, with or without prior sedation, produces stress responses. Some atopic cats are as reactive as any dog but whether this has any prognostic significance is yet to be determined (Muller *et al*. 2001). Treatment is usually required for life. A flea control program should be instituted to prevent fleabites from aggravating the pruritus. Pruritus can be controlled with immunosuppressive drugs and immunotherapy. Systemic antihistamines can reduce the clinical signs in 40% to 70% of atopic cats. They can be used in combination with glucocorticoids and essential fatty acids. A beneficial effect should occur within 1 to 2 weeks. Systemic glucocorticoids are effective and inexpensive controlling pruritus in most cases. Chronic usage can carry severe side effects (e.g. iatrogenic Cushing's, diabetes mellitus, pancreatitis and renal failure). Although cats appear relatively resistant to the acute and chronic side effects of glucocorticoids, probably because of their decreased number of glucocorticoid receptors (Muller *et al*. 2001). Long-term side effects of prednisolone may be a reason for seeking alternative medication. Cyclosporine (CsA) was found to be a valuable alternative to prednisolone without serious side effects. It was seen to have equal or better effect on pruritus and cutaneous inflammation. No significant difference was noticed in remission or in the number of cats that improved between the CsA group and the prednisolone group. There was also no difference in response to either CsA or prednisolone when comparing the subgroups of cats with or without immediate skin test reactivity to one or more allergens. This reflects the recognized inconsistency of skin testing in cats (Wisselink & Willemse 2009). Allergen specific immunotherapy can be used when the IDST or the serum allergen-specific IgE tests were successful in identifying allergens. Allergens with positive scores should be included in the allergy treatment serum. Allergen specific immunotherapy is reported to be successful in 60 to 78% of cases and the incidence of side effects is low (Trimmer *et al.*2006) However, most studies included small numbers of cats and do not involve long-term follow-up. Additional medications on an intermittent or continual basis may be required. Cats can improve within a month or in 1 year (Trimmer *et al*. 2006). Linear eosinophilic granulomas and indolent ulcers tend to respond better than self-induced alopecia (Muller *et al*. 2001). There is no absolute answer to when to discontinue the vaccines. Pruritus scores, dose and frequency of additional medications may monitor improvement (Trimmer *et al.*2006). Pat´s serum allergy test results were not very exuberant but were thought to correlate well with the

patient's seasonal exacerbation, and immunotherapy was pursued. The identified allergens were used to produce a vaccine that hopefully will control his pruritus and wean him out of CsA and antihistamines. No information in cats was found regarding the influence of the administration of CsA over the test results. Also, the fact that the restriction diet was not maintained for a minimum period of 6-8 weeks compromised its interpretation.

The prognosis for feline atopy is guarded for the cure without hyposensitization but good for remission of clinical signs with medical treatment, although some cases are extremely difficult to manage. Concurrent fleabite hypersensitivity, food hypersensitivity, and secondary bacterial pyoderma greatly interfere with achieving a favorable therapeutic response, and care should be taken to alleviate these complications (Muller *et al*. 2001).

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Signalment and reason for consultation: Marcy is a 4-year-old Female spayed American domestic shorthair cat that was presented to UTCVM's Oncology Service for a 1-month post-splenectomy recheck and consideration for chemotherapy for her mast cell disease.

Anamnesis: Marcy was initially presented to UTCVM Oncology service for further evaluation of multifocal cutaneous mast cell tumor (MCT), diagnosed by the referring veterinarian via skin biopsy. On presentation, Marcy had multifocal red, raised, ulcerated cutaneous masses ranging from 1mm-5mm throughout her body, including the face, head, neck, legs, trunk, back, ventrum. The owners reported that she was intensely pruritic (10/10) and unable to sleep well. Diagnostic work-up by the Oncology service included repeat skin biopsy (that confirmed MCT) and staging. CBC was within normal limits and the chemistry panel showed no abnormalities. On chest radiographs there was no evidence of pulmonary metastasis. Abdominal radiographs had no visible masses in the abdominal organs but multifocal soft tissue nodules were noted throughout her skin. Marcy´s abdominal US showed enlarged spleen. Fine needle aspirates of the spleen were collected and cytology was consistent with MCT. Marcy underwent splenectomy as well as ileocecocolic lymph node biopsy and liver biopsy for more complete disease staging. There were no intraoperative complications. The liver and ileocecocolic lymph node had no mast cell infiltration but the spleen biopsy confirmed diffuse splenic mast cell tumor.

One month after surgery Marcy re-presented with multifocal, raised, ulcerated, hyperemic, alopecic, pruritic nodules of unchanged size and location. Some nodules may have looked less swollen than pre-surgery. The owner mentioned that Marcy's pruritus decreased (5/10) and that her energy levels increased. She also stated that after surgery some nodules began disappearing but a week before presentation she started developing new nodules (especially on the head) and became progressively itchier. Marcy was dewormed and up to date on vaccines. She was a strictly indoor cat, and had no other animal housemates. She ate medium quality moist diet, and had ad libitum dry food of the same quality. Marcy had no contact with toxic waste or garbage and was currently being medicated with: Famotidine 1mg/kg PO sid and Cetirizine 1mg/kg Bid.

Physical Examination: Marcy was alert and bright showing a normal behavior. Her body condition Score (BCS) was 9/9, and she weighted (6,13 Kg). She had normal respiratory rate (24 rpm) and effort (her respiratory movements were costo-abdominal, regular and the relation between inspiration and expiration was 1:1.3, with no use of the accessory muscles of respiration), and also had normal lung and heart sounds. Bilateral, symmetric, strong and synchronic pulses with a frequency of 180 p.p.m were palpated. She had pink and moist mucous membranes with a CRT <2 sec. Her rectal temperature was 39ºC, and no parasites or blood were seen on the thermometer. The anal tone was normal. A dehydration degree of <5% was observed in the patient. All lymph nodes were within normal limits. Abdominal palpation did not reveal any abnormalities but as Marcy was tense and obese. Multiple skin lesions were

found on the skin of the head, body and extremities. They were multifocal, raised, some ulcerated, hyperemic, and alopecic. Marcy was pruritic on physical examination.

Problem List: Pruritus 5/10; Multifocal raised, ulcerated, hyperemic, alopecic skin nodules;

Differential Diagnosis: Multiple cutaneous mast cell tumor (diffuse cutaneous mastocytosis), urticarial pigmentosa, mastocytic dermatitis of allergic etiology, epitheliotropic lymphoma and progressive feline histiocytosis.

Diagnostics: CBC, chemistry panel with electrolyte and urinalysis were within normal ranges.

Diagnosis: Feline diffuse cutaneous mastocytic mast cell tumor with spleen involvement.

Treatment: Famotidine 0.8mg/kg PO sid, Cetirizine 0.8mg/kg Bid, Masitinib 50 mg PO sid, Predniosolone 0.8mg/kg PO sid.

Assessment: MCT´s are the second most frequent cutaneous neoplasia in the cat. They are classified histologically as mastocytic MCT and histiocytic (atypical) MCT. The first is more common and histologically similar to the MCTs in dogs. The histiocytic MCT form is very rare and mast cells comprise only 20% of the cells present. For this reason it can be misdiagnosed as granulomatous nodular paniculitis or deep dermatitis. Spontaneous regression can occur over a period of 4-24months. (Tham & Vail 2007)

The mean age for MCT occurrence is 8-9 years, there is no confirmed sex predisposition however in a Sabatini & Bettini study males had a higher prevalence although sex was not correlated with outcome (Sabatini & Bettini 2010). Siamese cats appear to be predisposed to the development of MCTs of both histologic types (Tham & Vail 2007).

The mastocytic MCT can be either compact (well differentiated) or diffuse (pleomorphic). The compact form accounts for 50% to 90% of cases and is associated with more benign behavior. The diffuse form is uncommon and behaviorally more malignant.

The majority of feline cutaneous MCT are behaviorally benign with the metastatic potential ranging from 0 to 22%. The cases that do develop metastases are the ones with diffuse mastocytic form of disease. When present, systemic involvement has a poor prognosis and may have a fatal outcome (North & Banks 2009). Cats with solitary cutaneous MCT were reported to survive longer that those with 5 or more nodules (Sabatini & Bettini 2010).

Visceral MCTs (splenic and intestinal) are more common in the cat than in the dog. Widespread dissemination and metastasis are also much more common. The intestinal MCT is the third most frequent intestinal tumor in cats after lymphoma and adenocarcinoma. It commonly involves the small intestine; colonic involvement is reported in less than 15% of cases. Lesions can be solitary or multiple. Metastases to the mesenteric lymph nodes and/or liver are frequent. Intestinal MCT is associated with widespread dissemination and has poor prognosis, most - animals die or are euthanized soon after diagnosis (Tham & Vail 2007).

Splenic MCT is the most common differential diagnosis for splenic disease in older cats (other differentials include: lymphoma, myeloproliferative disease, hemangiosarcoma, hyperplastic

nodules and adenocarcinoma) (North & Banks 2009). Studies have shown that 90% of metastasis occurs in the liver, 73% in the visceral lymph nodes, 40% in the bone marrow, 20% in lung and 17% in the intestines. One third of the patients can also present with peritoneal and pleural effusions rich in eosinophils and mast cells. Splenic involvement can be diffuse or less commonly nodular. It has been reported that approximately 18% of cats with cutaneous MCTs developed splenic metastasis. In contrast to dogs, cats with visceral intestinal form of MCT do not have concurrent cutaneous MCT, but metastasis and gastrointestinal ulceration are much more common (Tham & Vail 2007).

Marcy was diagnosed via biopsy with diffuse mastocytic pleomorphic cutaneous MCT with splenic involvement. Biopsy of the liver and ileocecal lymph nodes was performed and no mast cell infiltration was identified. Diffuse spleen involvement with low mitotic index was also noted. Anatomic location and form of feline MCT are known predictors of outcome. For example, diffuse pleomorphic cutaneous mast cell tumors are associated with poor prognosis. High mitotic index was associated with unfavorable outcome in Sabatini & Bettini study (Sabatini & bettini 2010). Although Marcy´s mitotic index was low, she had the disseminated cutaneous pleomorphic form of MCT.

A typical feline cutaneous MTC presentation is a solitary, raised, firm, well-circumscribed, hairless, dermal nodule measuring 0.5-3cm in diameter. Lesions are often white but a pink erythematous form can occasionally be seen. A pruritic, plaque-like lesion that resembles eosinophilic plaques or discrete subcutaneous nodules can occasionally be found. In 20% of the cases the nodules are multiple. Head and neck lesion involving the pinna, near the base of the ear are the most common sites for presentation. Trunk, limbs, and other miscellaneous sites are less commonly involved. MCTs rarely occur within the oral cavity. Intermittent pruritus and erythema are common. Self-induced trauma or vascular compromise may result in ulceration. Affected cats are otherwise healthy (Tham & Vail 2007).

Cats with disseminated forms of MCT can have systemic signs of disease. Depression, anorexia, weight loss and intermittent vomiting are associated with splenic and intestinal involvement. The presence of peritoneal effusion and splenomegaly is suggestive of splenic MCT. Cats with intestinal MCT can present with fever, diarrhea with or without bloody stools and they are usually ill for several months. Signs related to the release of vasoactive components of mast cell granules, including gastrointestinal ulceration, uncontrollable hemorrhage, altered smooth muscle tone, hypotensive shock and labored breathing can be observed with systemic forms and have episodic nature. Increased expiratory effort can also be seen secondary to pleural effusion or anemia, which is present in one third of patients with disseminated disease (Tham & Vail 2007).

FNA cytology is usually diagnostic. This includes FNA of cutaneous lesions, splenic aspirates, thoracocentesis and abdominocentesis if pleural or peritoneal effusions are present. Intestinal

mass aspirates are less frequently diagnostic. Tissue biopsy and histological assessment is needed to diagnose the cutaneous histiocytic form of MCT (Tham & Vail 2007).

After obtaining histopathologic description, clinical staging is important to determine the extent of disease, prescribe the most appropriate treatment, and provide prognostic information. A complete blood count (CBC), serum biochemistry and urinalysis should be performed as base line diagnostics. Cats with visceral disease can be anemic and 50% have bone marrow involvement. Cats with splenic disease can have a striking peripheral mastocytosis (>32.000cells/uL). Hyperglobulinemia has also been reported but the cause is still unknown. Imaging with thoracic and abdominal radiographs can confirm pleural or peritoneal effusions. Abdominal ultrasound helps determine the extent of visceral dissemination, but a laparoscopy or a laparotomy may be needed to get a definitive diagnosis in cats with intestinal form of disease. For cats with intestinal MCT, ultrasound can be used to delineate the mass and stage for regional or distant metastasis. Peripheral mastocytosis is not usually associated with intestinal MCTs but eosinophilia has been reported (Tham & Vail 2007).

Feline MCTs are suspected to have similar carcinogenic mechanism as in dogs. A c-kit gene mutation on exon 8 in the extracellular ligand-binding domain has been reported in the cat. The c-kit gene encodes for KIT receptor tyrosine kinase, which is a transmembrane protein that consists of several immunoglobulin-like domains (IgDs): an extracellular domain, a transmembrane domain, and a cytoplasmic kinase domain. The latter is split by a kinase sequence insert into adenosine triphospfate (ATP) binding domain and a phosphotransferase domain. The KIT protein is expressed in a variety of different tissues and mediates pleiotropic biological effects through its ligand – stem cell factor (SCF). A gain-of–function mutation in the c-kit gene, which is the protooncogene encoding KIT, has been demonstrated to be associated with the pathogenesis of acute myeloid leukaemia, gastrointestinal stromal tumour and mastocytosis in humans by inducing constitutive ligand-independent kinase activation (Isotani *et al.*2006). In Sabatini & Bettini study, high KIT immunopositivity, as well as high mitotic and proliferative indexes were associated with unfavorable outcome (Sabatini & Bettini 2010).

Surgery is the treatment of choice for the focal mastocytic form of feline cutaneous MCT. Since these lesions are behaviorally benign large margins are not needed, which is fortunate since these tumors tend to be located on the head. The incidence of local recurrence after surgical excision ranges from 0-24%, the systemic spread varies from 0-22%. If recurrence happens it is usually within 6 months of surgery. The histiocytic form has been reported to regress spontaneously, and a “wait and see” approach may be taken when it is found in young cats with multiple lesions (Tham & Vail 2007). In cases of diffuse cutaneous mastocytic tumors, like seen in Marcy´s case, surgical approach is often not feasible, due to the extent of disease, and chemotherapy is needed the only reasonable treatment option. However, the efficacy of chemotherapy in feline MCT has not been well established (North & Banks 2009)

Cats with splenic MCT are reported to greatly benefit from splenectomy. Even in cases with bone marrow and peripheral blood involvement, long term survival (12 to 19 month), with good quality of life is described. However, anorexia and progressive weight loss are associated with worse prognosis (Tham & Vail 2007). Marcy was seen to improve after surgery. She had less pruritus and some nodules started to disappear. However, in the first month after surgery new nodules began to reappear and she was never pruritus-free.

Systemic treatments are needed for patients like Marcy, when surgery is not possible or has not been successful (eg, cats with cutaneous or intestinal MCTs that are not resectable or are metastatic or recurrent after splenectomy). The use of adjuvant systemic treatment might be helpful to improve tumor control and survival time following surgery. Rassnick *et al.* showed in a study of 38 cases that lomustine had antitumor activity and was well tolerated in cats with cutaneous MCTs when administered at a dosage of 50 to 60 mg/m2. The response rate was of 50% with a median duration of the response of 168 days. No response was seen in animals with splenic involvement. This paper supports the use of lomustine for treatment of cats with cutaneous MCTs when surgical treatment is not possible or has not been successful (Rassnick *et al.* 2006).

Lomustine is an alkylating agent. These agents bind DNA stands, insert an alkyl group, and cause DNA breaks. Lomustine is usually used in lymphoma, and histiocytic sarcoma treatment. It is moderately expensive and toxic when compared with other drugs (Tham & Vail 2007), but its toxic effects in cats have not been well-defined. One study showed neutropenia as a dose-limiting toxic effect. This was suggested to be a cumulative myelotoxicity that may occurs in cats receiving lomustine long term. Hepatic damage due to lomustine usage is reported in dogs. Although it was not identified in the cats in the Rassnick et al. study, there was no adequate follow-up time to draw meaningful conclusions. Two of the cats receiving lomustine developed pleural effusion. Because of those findings, cats on lomustine treatment should be carefully evaluated for cumulative myelosuppression and organ damage (Rassnick *et al.* 2006).

Isotani *et al.* in 2006 identified for the first time the presence of c-kit mutation in a cat diagnosed with systemic mastocytosis. The same cat was underwent treatment with the tyrosine kinase inhibitor, imatinib mesylate, at a dose of 10mg/kg/day PO for 5 weeks without any additional treatments such as chemotherapy or steroids. The animal had a dramatic improvement, in 3 weeks the masses were reduced in size and in 5 weeks they were no longer detectable. The number of mast cells in peripheral blood had also decreased in 2 weeks but in 5 weeks the count was up to 40cells/uL (Isotani *et al.* 2006). In another study of 10 cats (2009 Isotani *et al.)* it was found that c-kit mutations were present in 70% of animals. Approximately 65% of cats had a mutation in the fifth immunoglobulin domain (IgD), which is different from the dog, where mutations are more frequently present in the juxtamembrane domain followed by the fifth IgD. Isotani *et al.* concluded that the mutations in the fifth IgD might be critically involved in the

pathogenesis of MCTs in cats. Of the 8 animals that had c-kit mutations, 7 responded to treatment with imatinib. Six achieved a partial remission (at least 30% decrease in the sum of the longest diameters of target lesions) and one achieved complete remission (disappearance of all target lesions) (Isotani *et al.* 2009).

Although very limited information is available about the effectiveness of tyrosine kinase inhibitors for the treatment of MCTs in cats, Marcy was started on masitinib at the recommended dose of 50 mg PO sid. Prednisolone was used at a dose of 0.8mg/kg PO sid in order to address Marcy´s pruritus. Prednisolone was also used as chemotherapy drug because it binds to the cytoplasmic receptors in mast cells and inhibits DNA synthesis (Tham & Vail 2007).

More studies are needed to determine c-kit's role in feline MCT oncogenesis, and investigate c-kit expression levels, and KIT protein localization as prognostic indicators. More studies are also needed to explore c-KIT as target for therapy with tyrosine kinase inhibitors. Efficacy and toxicity of these drugs in cats still needs investigation. The existing studies have a small numbers of cats and therefore the conclusions are only preliminary.

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Signalment and consult motif: Bubba is an 8 years old male castrated Jack Russell Terrier that was referred to the anesthesiology service of UTCVM by the cardiology service of the same institution in order to be anesthetized for a pacemaker implantation.

HISTORY: Bubba had been presented to the cardiology service for evaluation of recurrent episodes of syncope that started at least 1 month before. They did not have any obvious trigger. When it happened Bubba slumped over to his side and within 2 minutes, he was back to normal. Previous CBC and ECG made by the referring veterinarian were been normal. Bubba had one episode at his referring veterinary clinic and an atrio-ventricular block and ventricular escape beats were seen on ECG. He was referred to the UTCVM in order to be submitted to an echocardiogram and a Holter monitorization. Bubba lived in a house with private exterior access and has no contact with other animals. He did not contact with garbage or toxic waste. He was currently dewormed and vaccinated. His diet was based on premium quality dry food. No other abnormalities were noticed when questioned about the different systems and there was no relevant previous medical history and was not receiving any medication.

PHYSICAL EXAM: Bubba was alert and showing a normal behavior. His body condition score (BCS) was 5/9, and weighted 8,0 Kg. Normal respiratory rate (40 rpm) and effort; normal lung sounds. Heart auscultation showed an irregular rhythm (physiologic sinus arrhythmia seen on echo ECG timing lead) and no murmurs or gallop sounds. Bubba had bilateral, symmetric, strong and synchronic pulses with a frequency of 110 p.p.m. Pink and moist mucous membranes CRT < 2 sec were observed. His rectal temperature was 39ºC, and no parasites or blood were seen on the thermometer, a normal anal tonus was also observed. His dehydration degree was <5%. All lymph nodes were within the normal limits. No abnormalities were found in his abdominal palpation.

PROBLEM LIST: Syncopes, atrio-ventricular blocks and escape beats.

DIFERENTIAL DIAGNOSIS: Myocardical failure; Arrhythmias (bradyarrhythmias: high grade second degree heart block; sick sinus syndrome; third degree heart block or tachyarrhythmias: Supraventricular tachycardia, ventricular tachycardia); Obstructions to cardiac inflow or outflow (valve stenosis, pulmonary hypertension, cardiac tamponade, cardiac masses); Hypoxaemic disease; Neurological dysfunction, metabolic disorders and myopathies.

DIAGNOSIS: Echocardiogram: Normal heart chamber sizes and wall measurements; normal left atrial pressure estimate; normal systolic and diastolic function; mild thickening of mitral valve. All other valves were normal, no regurgitations and normal outflow tract velocities. physiologic sinus arrhythmia seen on echo ECG timing lead. Holter: recorded for 25h 30m and with very good quality. The average heart rate was 65 bpm, with a maximum rate of 255 bpm at 2:58pm (while traveling). The minimum rate was of 30 bpm at 1:58am (while asleep). There were 6,621 pauses > 2s, with the longest being 6.86s at 9:25am. Throughout the recording period, there were 761 single ventricular complexes, but these were all escape beats (no

ventricular premature complexes seen). No supraventricular ectopic beats were seen. CBC, chemistry panel and electrolytes: All values were within the normal ranges.

DIAGNOSIS: Sick Sinus Syndrome (SSS).

Treatment: Pacemaker implantation

Anesthesia procedure: Bubba was given butorphanol (0,4 mg/kg IM) to provide sedation to catheter placement 4 hours before premedication because the patient arrived early.

The patient was premedicated with fentanyl (5 mcg/kg IV), and glycopyrrolate (0,01 mg/kg IM) 30 min before induction was started. Transthoracic pacemaker leads were placed in case severe bradycardia occurs during induction. Midazolam (0,5mg/kg, IV) and ketamine (5mg/kg, IV) combined in the same syringe were administered for anesthetic induction. Propofol (4mg/kg, IV) was administered as a co-induction to effect, until intubation with a 7,0 mm cuffed endotracheal tube was possible. Bubba became apneic and was connected to a ventilator using a circle anesthetic circuit. Respiratory rate of 9 breaths/min using a tidal volume of 15ml/kg was necessary to maintain the patient normocapnic (35-45mmHg). An initial end-tidal 2.5% sevoflurane concentration was maintained using 2.0 L/m oxygen flow. Anesthesia was maintained with sevoflurane at a median percentage of 2.0% in 1.3L/m of Oxygen and a constant-rate infusion of fentanyl (10mcg/kg/hr IV). Fluid therapy was performed with a continuous crystalloid infusion of 5ml/kg/hr Plasma-lyte®.

Oxygen saturation was measured by pulse oximetry (SpO2). End-tidal pressure of carbon dioxide (ETCO2) and temperature were monitored with a multiparameter anesthesia monitor. Arterial catheter placement was unsuccessful and blood pressure was measured with a non-invasive blood pressure (NIBP) monitor. A lead II ECG was monitored continuously for changes in heart rate and rhythm. Immediately after anesthesia was induced, SpO2 was 98%, ETCO2 was 49mmHg and rectal temperature was 37ºC. Pulse rate was 70ppm. No abnormalities were observed on ECG during the procedure. Systolic blood pressure was initially 99 mmHg, mean was 75mmHg and diastolic was 60mmHg. Those values maintained relatively constant during surgery and no anesthetic complications were identified. Cefazolin (22mg/kg) was given IV every 90min. For pain management carprofen (4mg/kg SC) was administered before the end of anesthesia. Bubba recovered calmly from anesthesia.

Assessment: Disorders of the sinus node are known as sinus node dysfunction or SSS that result from an inadequate impulse formation or conduction. This disease primarily affects the sinus node, but abnormalities of the AV conduction system may coexist causing prolonged periods of assystole and failure of appropriate escape rhythm generation. (Vailati *et al*. 2011) When the sinus node fails to propagate, the junctional tissues of the heart should depolarize. Abnormalities related to SSS pauses of various durations (can last up to 10 seconds) without P waves or an escape rhythm. Older female Miniature Schnauzers and west Highland Terriers are commonly affected. Syncope is a common complaint. Some dogs do not manifest clinical signs

but bradycardias are noticed in routine examination. The prevalence of subclinical SSS is unknown. Sinus pauses can be occasionally captured in lead II ECG but in many cases a Holter monitoring is necessary to have a diagnosis (Tilley *et al.* 2007). Permanent pacemaker implantation is the ideal treatment for SSS. Pharmacologic therapy is usually of limited value. Parasympatholytic (atropine and glycopyrrolate) or sympathomimetic drugs (isoproterenol and dobutamine) are used in hope of increasing the ventricular response and reducing the clinical signs related with severe bradycardias but long-term control is disappointing (Tilley *et al.* 2007).

Bubba`s collapse episodes had characteristic consistent with cardiac syncope (brevity, no pre or post-ictal period). Cardiac syncopes can be due to arrhythmias, obstructions to cardiac inflow or outflow. The fact that no abnormalities were identified in the echocardiography ruled out many of these possibilities. A Holter was performed and the presented pauses were long enough to be considered cause of syncope. SSS was diagnosed based on long enough pauses (> 2s, longest: 6.86s) and the fact that all 761 single ventricular complexes were escape beats. Because these pauses pose a mild to moderate risk for syncope or sudden death if untreated, a pacemaker implantation was done. To do so, the anesthesiology service was requested to perform anesthesia.

The anesthetic management of a patient with cardiovascular dysfunction can be very challenging, since most preanesthetic and anesthetic agents are capable of CNS depression and also capable of producing cardiovascular depression. Patients with cardiovascular dysfunction may be more prone to fluid overload and dysrhythmias. Extremes in heart rate may cause severe problems, including heart failure. Patients with cardiovascular dysfunction may lack sufficient cardiac reserve to compensate for anesthetic induced depression. There can be no single suggestion as an anesthetic management techniques or protocol for all animals with underlying cardiovascular dysfunction (Seymour & Novakovski 2007). Each individual must be assessed with regard to cardiovascular pathophysiology, coexisting systemic or metabolic diseases, hemodynamic effects of surgical procedure, influence of anesthesia on the cardiovascular system, and potential interactions between the anesthetic and concurrent medications (Tilley *et al.* 2007).

The decision whether a patient with heart disease should or not be anesthetized begins by classifying the patient according to its functional heart failure. The International Small Animal Cardiac Health Council provided guidelines for 3 functional classifications of heart disease that are based on clinical signs. This classification does not differentiate the type of heart disease but provides decision-making guidelines based on the clinical presentation. This classification is combined with the classification of physical status for anesthetized patients adopted by the American Society of Anesthesiologists (ASA) to assess the anesthetic risk and aid in choosing the safest protocol. There are 3 functional grades. The first is the asymptomatic patient with a confirmed heart disease but is not presenting clinical signs of heart failure. Those patients can

be safely anesthetized without further stabilization. The second classification describes patients with mild to moderate clinical signs of heart failure that are evident at rest or with mild exercise. Stabilization of clinical signs and the absence of those for several days with drug therapy are recommended prior to sedation or anesthesia. When patients of this group need a life-saving emergency surgery, they should have parenteral cardiac drug therapy instituted immediately by and clinical signs controlled as much as possible before and during anesthesia. The third grade corresponds to immediately obvious advanced clinical signs of heart failure. Patients severely affected can present in cardiogenic shock and death or severe debilitation is likely without therapy. Anesthesia is contraindicated in this third category of patients until clinical signs are stabilized with aggressive drug therapy. Owners should be advised of the increased risk of death or severe debilitation during or immediately after anesthesia (Tilley *et al.* 2007). According to this classification, Bubba was considered to be in the second group because he had a dignosed heart disease and he presented clinical signs (syncopes) The anesthetic risk classification can be determined based on physical status (Annex IV-1). Five categories have been developed. Unstable patients with clinical signs of cardiac decompensation and heart failure are classified as ASA IV and should not be anesthetized until the disease is stabilized. Patients in the ASA V category are the ones with a long history of heart disease that is refractory to all cardiac drugs. If stabilization of heart failure is not possible, death during anesthesia is likely (Tilley *et al.* 2007). Bubba was considered an ASA IV patient because his heart disease could cause him cardiac arrest in any time and bradycardias needed to be avoided. However he did not have any systemic signs.

Premedication has a major impact on the characteristics of the ensuing general anesthesia. Making the appropriate selection of drugs concerning each individual can significantly improve intraoperative cardiovascular stability, perioperative analgesia and quality of recovery (Seymour & Novakovski 2007). In Bubba´s cas, the major concern was to avoid bradycardia. At very low heart rates, reduced cardiac output and coronary arterial flow may lead to cardiac arrest. In order to avoid it, it is important to choose a pre-anaesthetic medication that does not reduce heart rate nor increases systemic vascular resistance (Seymour & Novakovski 2007).

Because opioids are very attractive drugs to be used in patients with heart disease (they do not affect myocardial contractility or vascular tone) fentanyl, a pure Mu agonist opioid, was used (Tilley *et al.* 2007). When administered IV, fentanyl has a fast onset (1-2min) and shot duration of action (20-30min). In pain-free dogs like Bubba, doses in the range used to control pain generally result in recumbency and sedation. (Seymour & Duke-Novakoski 2007) Glycopirrolate, a quaternary ammonium anticholinergic agent, was used as a premedication drug in order to prevent the unwanted effects of parasympathetic nervous system caused by anesthetic agents or surgery. Glycopyrrolate has a vagal inhibition of 2-3hours (Seymour & Duke-Novakoski 2007).

For the Induction, a combination of midazolam (0.5mg/kg, IV), ketamine (5mg/kg, IV) and Propofol (4mg/kg, IV) was used. Midazolam, was elected to be used due to benzodiazepines minor effects in the cardiovascular and respiratory systems. Benzodiazepines produce minimal sedation in healthy dogs and therefore are combined with other sedatives. The combination of benzodiazepines with ketamine is a stable cardiovascular combination. The administration of a low dose of ketamine is a strategy to manage low heart rates because it has sympathomimetic properties. Ketamine is a dissociative agent with a very fast onset of action (30-90 sec). It produces a dose-dependent CNS depression that leads to a dissociative state, characterized by profound analgesia and amnesia with maintained ocular, laryngeal and pharyngeal reflexes. Ketamine anesthesia is associated with increased muscle tone, muscle spasm and seizures. The combination with midazolam helps to reduce these side effects and to obtain a surgical state of anesthesia. The main reason for the choice of ketamine was its unique cardiovascular effects due to the central stimulation of the sympathetic system. Unlike other intravenous anesthetics, it stimulates the cardiovascular system, resulting in increases in heart rate, blood pressure and cardiac output. However, this raise in hemodynamic variables is associated with an increased myocardical work and oxygen consumption. A healthy heart can enhance its oxygen supply by coronary vasodilatation and increased cardiac output but in compromised hearts (hypertrophic) may not be able to mount such response (Seymour & Duke-Novakoski 2007).

Propofol is a hypnotic agent with a rapid onset (60-90sec) and short duration of action (10 min). Its hypnotic action is mainly mediated by interaction with the GABAA receptor subunit, potentiating the GABA-induced chloride current. The most prominent hemodynamic effect of propofol is moderate hypotension due to reduction in cardiac output and systemic vascular resistance. In patients with pre-existing bradycardias, like Bubba with his SSS, refractory bradicardia or asystole can occur. For this reason transthoracic pacemaker leads were placed before propofol administration and a low dose was used (4mg/kg; dose range. 2-6mg/kg). The administration of glycopyrrolate and ketamine was also a preventive procedure to avoid refractory bradycardias and hypotension. Respiratory depression can be caused by the rapid injection of propofol. (Seymour & Duke-Novakoski 2007) This was observed in Bubba and he was connected to a ventilator troughout the entire procedure.

A balanced anesthesia was performed using a volatile agent (Sevoflurane) and a continuous rate infusion of fentanyl. The analgesic and anaesthetic-sparing properties of this combination allows for the reduction of the concentration of volatile agents hence less cardiovascular depression. (Seymour & Duke-Novakoski 2007) Sevoflurane, a fluorinated ether less potent than isoflurane, was chosen for Bubba´s anesthesia. Due to the sevoflorane lower solubility, when compared with isoflurane, faster changes in the depth of anesthesia are possible. The cardiovascular depression is similar to that observed with isoflurane, but the degree of

respiratory depression is less profound with sevoflurane. (Seymour & Duke-Novakoski 2007). Bennett *et al.* (2008) compared the anesthetic characteristic of sevoflurane and isoflurane under routine veterinary clinical conditions by studying, 108 dogs. The dogs did not receive the same premedication nor induction protocol. The cardiovascular and respiratory functions were generally similar in the two groups. However there was a range of different premedication protocols, a wide range of dog sizes and breeds and different procedures were undertaken, facts that may have obscured small differences between the two groups. Both isoflorane and sevoflurane decreased arterial systolic blood pressure by the reduction of systemic vascular resistance. The respiratory effects were also fairly the same but in this specific study sevoflurane caused more respiratory depression than isoflurane. (Bennett *et al.* 2008)

Fentanyl and midazolam are frequently administered as constant rate infusions to reduce inhalant anesthetic requirements and subsequent unwanted hypotension (Saunder et al.2009). Saunder et al. (2009) measured the cardiac troponin I and C-reactive protein concentrations in 20 dogs, in order to study the myocardial injury caused by ischemia during anesthesia using sevoflurane or its combination with fentanyl and midazolam. In Saunders study fentanyl and midazolam when used in combination with sevoflurane had anesthetic sparing effect by requiring less volatile anesthetic to maintain an appropriate plane of anesthesia. However, when it comes to the comparative protective myocardical effects of those two protocols, conclusions are still to be determined and further studies are needed (Saunders *et al*. 2009). Bubba´s anesthesia was maintained with a low end-tidal sevoflurane (2.0%) which is an under the 2.4%, sevoflurane MAC. This protocol showed to be a successful approach in this case because neither bradycardias nor hypotension were observed.

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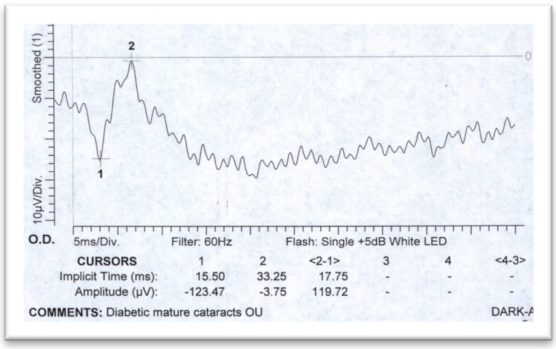
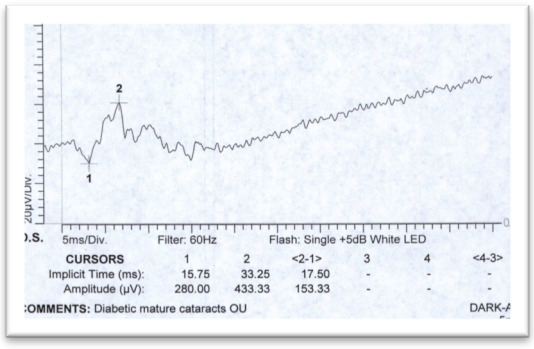
Appendices

Appendix I: Ophthalmology Appendix

1. **1.** Spice ERG:

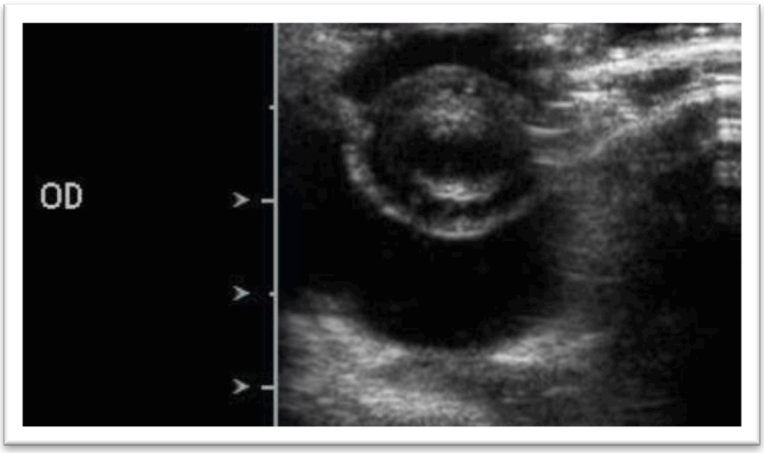


Right eye (OD)

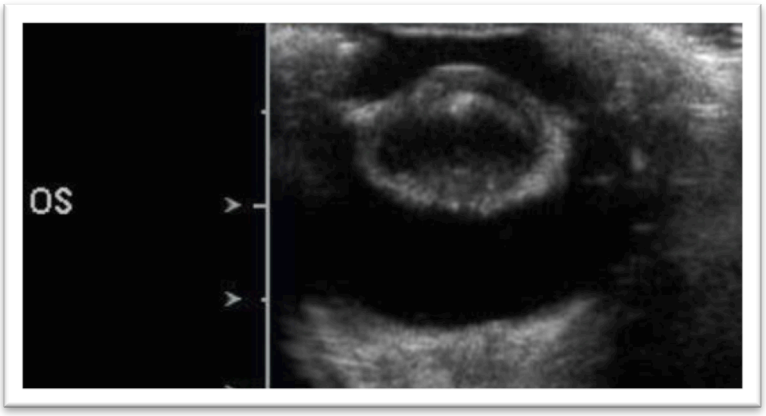


Left eye (OS)

2. Spice´s US OD and OS: Bilateral primary intumescent cataracts. Shallow anterior chambers OU. No retinal detachment was noticed.



Right eye (OD)



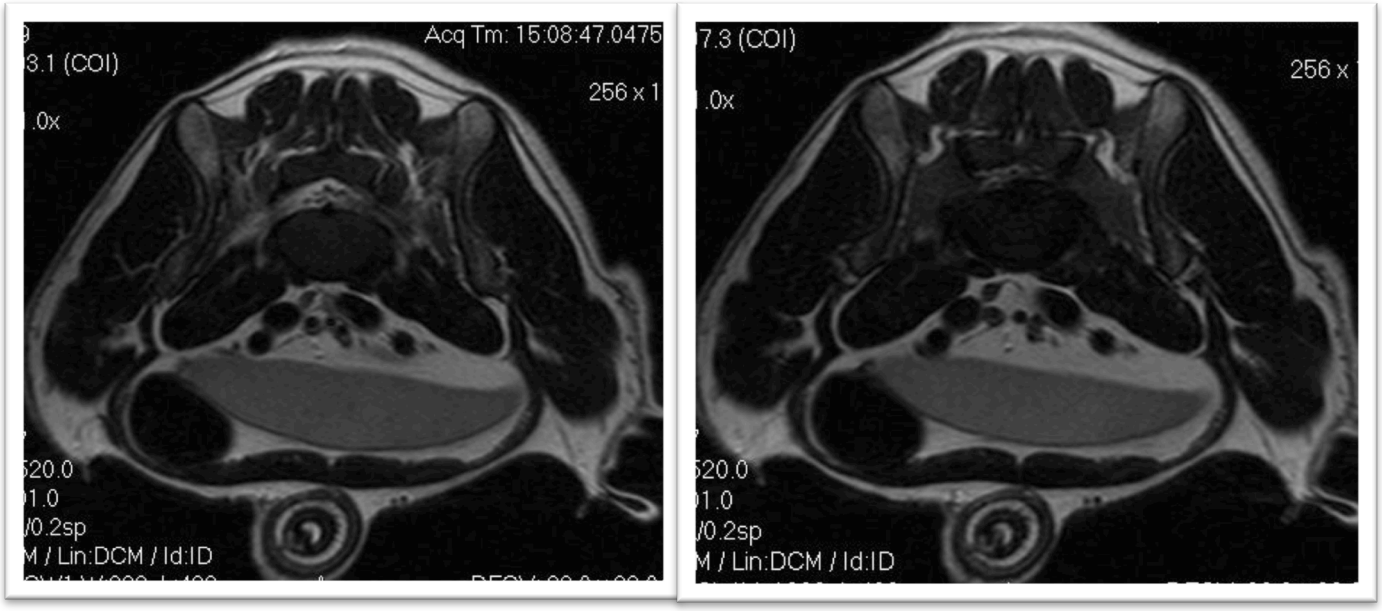
Left eye (OS)

Appendix II: Neurology Appendix:

1.Quanto´s hip joint. Ventro-dorsal projection. No Abnormalities

2.Osteochondrosis of the cranial endplate of S1, normal intervertebral spaces. Left lombo-sacral vertebral column.

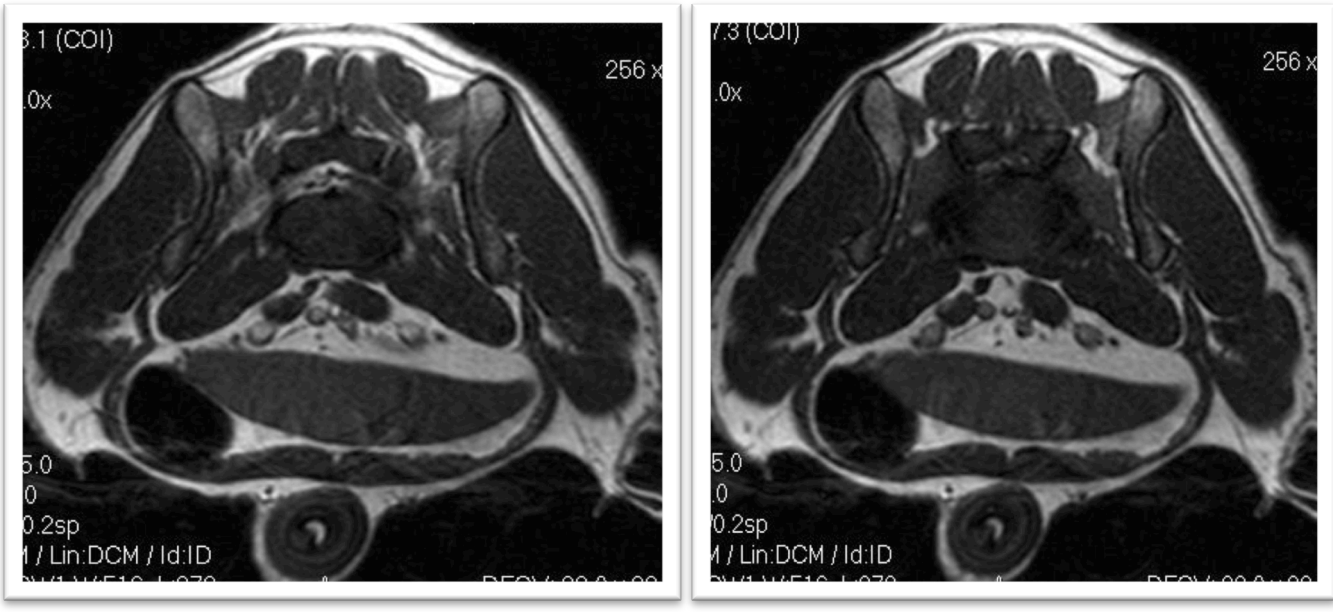
3.T2 transverse sequence: comparison between L6-L7 (image A) and L7-S1 (image B). Loss of epidural fat and spinal roots compression is visible in L7-S1. The left side spinal roots are more compressed than the right side spinal roots.



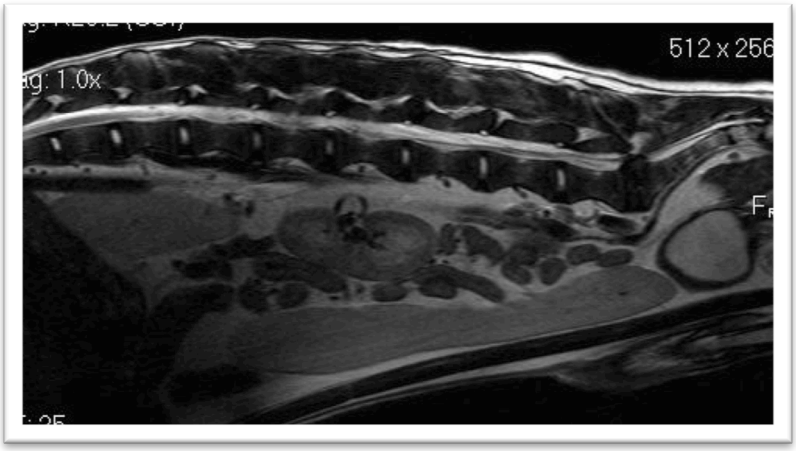
T1 transverse sequence: comparison between L6-L7 (image A) and L7-S1 (image B). Loss of epidural fat and spinal roots compression is visible in L7-S1. The left side spinal roots are visible more compressed than the right side spinal roots.

Image A

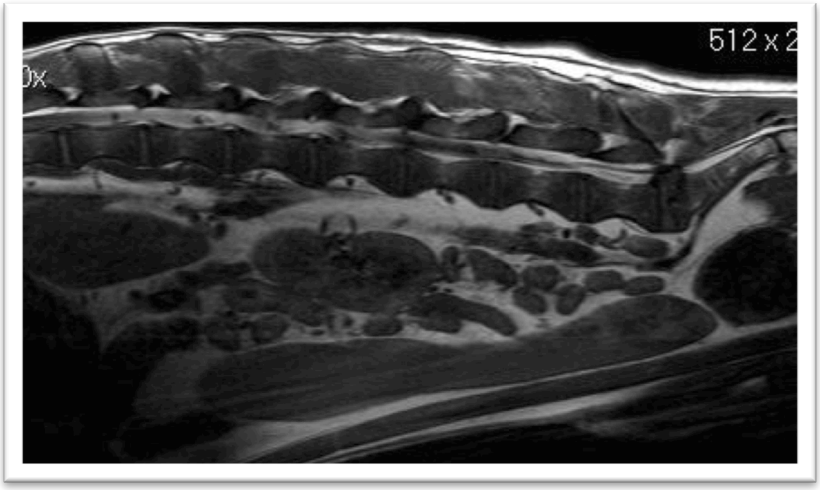
Image B



T2 Sagittal Sequence: compression of L7-S1 by hypointense tissue (Hansen II disc herniation). All the intervertebral discs are well-hydrated except for the L7-S1 IVD:



T1 Sagittal Sequence: extradural compression of L7-S1:



Proton weight density transverse sequence: Ovoid fragment at the craniodorsal aspect of S1, lying in the left ventral aspect of the vertebral canal. Circled in image B and not circled in A.

Image A

Image B

Appendix III: Anesthesiology Appendix:

1. Classification of physical status for anesthetized patients:

ASA Category	Description of Physical Status	Example
I	Normal, healthy	No cardiac disease, elective surgery (spay, castration)
II	Mild systemic disease	Compensated heart disease (no cardiac medications), fracture without shock
III	Severe systemic disease	Compensated heart disease (cardiac medications), anemia, fever, compensated renal disease, dehydration
IV	Severe systemic disease and a constant threat to life	Decompensated heart disease, electrolyte imbalance, uncontrolled internal hemorrhage
V	Moribund patient not expected to live with or without surgery	Decompensated heart disease refractory to cardiac drugs, terminal malignancy

Adapted by the American Society of Anesthesiologists.

2. Bubba´s Anesthesia Form: